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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,421	10/16/2003	Wei Han	PH 7474 NP	7985

23914 7590 03/13/2006

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,421	HAN ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 9-13* is/are pending in the application.

4a) Of the above claim(s) *9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/23/04; 12/5/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with travers of group II (claims 1-7 (in part) in the reply of 01-12-06 is acknowledged. The traversal is on the ground that: "The Office Action does not show or describe how Groups 1-14 "have different modes of operation, different functions, or different effects." " The traversal is not found persuasive for the following reasons:

1. The core of 'M-fused-pyrimidone' varies from quinazolinone to 5- or 6-membered heterocycle fused pyrimidinone. For instance, claim 4 lists 14 possible bicyclic systems represented by the 'M-fused-pyrimidone'. Those bicyclic systems further varies by J (representing heteroatoms). Thus, by the bicyclic systems recited in claim 4 alone, the claimed formula I represents at least 14 patentably distinct Markush groups.
2. Attaching to the variable core are substituents P_4 and M_4, which represent all kinds of rings or ring systems. Thus, the combination of P_4, M_4 and the variable core gives rise to well over 14 patentably distinct Markush groups. Therefore, the Markush group of formula I is improper.
3. As evident by the teaching of **Sadhu et. al.** (US 6,518,277), a compound of quinazolinone ring substituted with purine (a group corresponding to Z-A-B) does not have activity to treat thromboembolic disorder as alleged for the claimed formula I. Thus, as the core of formula I varies, the claimed compound would

definitely have different effect which undoubtedly would have different modes of action as well as different biological function.

Claims 1-7 and 9-13 are pending. There is no claim 8.

Claims 9-13 are withdrawn from consideration as being drawn to the non-elected subject matter.

Claims 1-7 are considered.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Scope of Enablement:** Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the make and use of compounds of formula I wherein P_4 is *pyridyl or phenyl* while M_4 is a *biphenyl* or *methoxy-phenyl*, does not reasonably provide enablement for the make and use of compounds of formula I wherein P_4 is another ring while M_4 is a *phenyl group substituted with a heterocycle*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims:

Claim 1 recites a formula I of a substituted pyrimidinone ring fused to ring M. The pyrimidinone part has two main substituents of P_4 and M_4. One of P_4 and M_4 represents –Z-A-B, while the other represents $-G_1$-G. The substituent of –Z-A-B represents countless combinations of divalent groups (Z), and ring or ring systems of A and/or B. The substituent of $-G_1$-G represents a myriad number of divalent groups (G), and various rings for ring systems of formula IIa or IIb defined for G. The ring (formula IIa or IIb) defined for G has substituent R, two of which could form a ring fused to either ring D or E (of formula IIa or IIb). Thus, G could also represent a tricyclic or tetracyclic system. Each of the group defined for G, G_1, Z, A, B and the substituent on M (i.e., R^{1a}) has variables (e.g., R^2, R^{2a}, R^3, R^7-R^9, etc.) that are further substituted with other variables (e.g., R, R^4, R^{4a}, R^5, R^6, etc.) which in turn represent several functional groups, rings or ring systems. Thus, the claimed formula I represents an extraordinary number of compounds, and not just substituted quinazolinone. Claims 2-6 depend on claim 1,

and still recite an extensive number of rings and functional groups. Claim 7 depends on claim 1, and recites species wherein P_4 is another ring while M_4 is a *phenyl substituted with a heterocycle.* Thus, the scope of claims 1-7 is unduly broad.

The amount of direction or guidance presented:

The generic scheme diagramed in Schemes 1-5 only provide guidance for the skilled chemist to make a quinazolinone compound having P_4 as a phenyl group, and M_4 also as a phenyl group. Examples 1 and 2 describe the process of making quinazolinone compound with P_4 as a pyridinyl group, and M_4 as a biphenyl or methoxyphenyl group. The specification does not teach how other compounds of formula I can be made even in a generic way, nor does it provide examples for species with M_4 as a *phenyl group substituted with a heterocycle* (recited in claim 7). Although the specification provides dosages for the claimed compound, there is no evidence if any compound of formula I has any biological activity. Thus, the specification fails to provide sufficient enablement for the large Markush group of formula I recited in claims 1-7.

The state of the prior art:

By the teaching of **Sadhu et. al.** (US 6,518,277 B1), the skilled chemist could obtain guidance for making and using compounds of quinazolinone substituted with phenyl or pyridyl at the 3rd position (or corresponding to P_4), and $-CH_2$-S-(substituted purine) at the 2nd position (or corresponding to M_4). However, the teaching of Sadhu et. al. would not allow the skilled chemist to make other compounds of the claimed formula I, or many species in the instant claim 7. Thus, the state of the prior art cannot remedy the deficiency in the enablement provided by the instant disclosure.

The relative skill of those in the art:

Even with the advanced training, the skilled clinician would have to carry out extensive research to make and select an effective compound from the large Markush group of formula I. Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50}, therapeutic index and pharmacokinetic profile for each compound. Given a large Markush group of the claimed formula I, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary:

The pharmaceutical art has always been unpredictable. Compounds of different rings or ring systems do not always share the same physical, chemical or biological activity. Note, even the same quinazolinone core disclosed by Sadhu et. al. has different biological activity from those of the claimed formula I. Thus, there is no logical rational to expect compounds of different cores in the claimed formula I to possess the same biological activity. With the limited teaching provided by the instant disclosure and state of the prior art, the skilled chemist would have to engage in undue experimentation to make and use compounds of formula I.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. In claim 1, the limitation of "*alternatively, when 2 R groups are attached to adjacent atoms, they combine to form methylenedioxy or ethylenedioxy*;" which has indefinite metes and bounds because it is unclear if these R groups forming a ring fused with ring D, ring E or both. Thus, it is unclear if group G could be a bicyclic, tricyclic or tetracyclic system.

b. The proviso of G is unclear as to what moieties can form with G the bond of "N-S, N-CH_2-N, N-CH_2-O, N-CH_2" because it is not evident such a bond present in groups represented by G.

c. The proviso of P is unclear for the reason stated above (or in item (b)).

d. The limitation of R^2 and R^{2a} forming a ring has indefinite metes and bounds because R^2 and R^{2a} are in the definition of X, and could be a repeating group. It is unclear if rings formed by R^2 and R^{2a} are connected in series (), or connected through carbon chain ().

e. Claim 2 lacks antecedent basis because it depends on claim 1 but recites Y as a bicyclic heteroaryl group which is not recited in claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over **Sadhu et. al.** (US 6,518,277 B1).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

On column 13, line 11, Sadhu et. al. disclose a quinazolinone compound of *2-(9H-pyrin-6-ylsulfanylmethyl)-3-pyridin-4-yl-3H-quinazolin-4-one.* The disclosed compound is analogous to a compound of the claimed formula I with the following substituents:

- P_4 is $-G_1$-G wherein G_1 is absent, and
- G is either formula IIa or IIb with D absent, and E is pyridyl;
- M_4 is –Z-A-B wherein Z is $-(CR^3R^{3a})_qS(CR^3R^{3a})_{q1}$;
- q = 1, and q1 = 0;

- A is a 9-membered heterocycle with 4 N's (or A is a purine);

The disclosed compound differs from the claimed compound by not having a substituent corresponding to the instant variable B. However, the compound on line 31 (column 13) shows that the *purine* can be substituted with an *amino* group, which corresponds to $-NR^2R^{2a}$ – a group defined for B of the claimed formula I. Furthermore, the preferred embodiment on column 9 shows that the generic formula (IV) allows the purine to be substituted with many groups represented by the instant variable B. Thus, there is an equivalent teaching for an unsubstituted purine and an amino-purine (corresponding to the instant variables A-B), which would motivate the skilled chemist to a quinazolinone compound of the claimed formula I with substituents cited above because said compound would have been expected to inhibit phosphatidylinositol-3-kinase delta isoform to treat disorders of immunity and inflammation.

Therefore, at the time that the invention was made, it would have been obvious to make and use some compound of the claimed formula I in view of the teaching above.

No pending claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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3-6-06

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